SMARCA4 gene

SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4

Normal Function

The *SMARCA4* gene provides instructions for making a protein called BRG1, which forms one piece (subunit) of several different SWI/SNF protein complexes. SWI/SNF complexes regulate gene activity (expression) by a process known as chromatin remodeling. Chromatin is the network of DNA and protein that packages DNA into chromosomes. The structure of chromatin can be changed (remodeled) to alter how tightly DNA is packaged. Chromatin remodeling is one way gene expression is regulated during development; when DNA is tightly packed, gene expression is lower than when DNA is loosely packed.

Through their ability to regulate gene activity, SWI/SNF complexes are involved in many processes, including repairing damaged DNA; copying (replicating) DNA; and controlling the growth, division, and maturation (differentiation) of cells. The BRG1 protein and other SWI/SNF subunits are thought to act as tumor suppressors, which keep cells from growing and dividing too rapidly or in an uncontrolled way.

The BRG1 protein uses a molecule called ATP, which provides energy for chromatin remodeling, although the exact mechanism of remodeling is unclear.

Health Conditions Related to Genetic Changes

Coffin-Siris syndrome

At least six mutations in the *SMARCA4* gene can cause Coffin-Siris syndrome. This condition is characterized by delayed development, abnormalities of the fifth (pinky) fingers or toes, and characteristic facial features that are described as coarse. The *SMARCA4* gene mutations involved in Coffin-Siris syndrome change single protein building blocks (amino acids) in or remove an amino acid from the BRG1 protein. Although it is unclear how these changes affect SWI/SNF complexes, researchers suggest that *SMARCA4* gene mutations result in abnormal chromatin remodeling. Disturbance of this process alters the activity of many genes and disrupts several cellular processes, which could explain the diverse signs and symptoms of Coffin-Siris syndrome. People with Coffin-Siris syndrome do not appear to have an increased risk of cancer (see below).

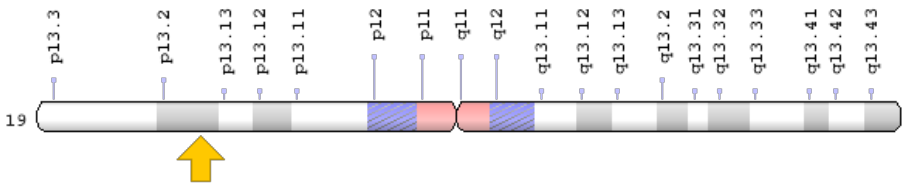
cancers

Mutations in the *SMARCA4* gene have been found in certain types of cancer, particularly lung cancer. These mutations are somatic, which means they are acquired during a person's lifetime and are present only in tumor cells. The mechanism by which mutations in the *SMARCA4* gene contribute to lung cancer is unknown, although it is thought that changes in SWI/SNF complexes are involved. These changes may impair normal cell differentiation, which leads to the overgrowth of certain cell types, causing cancer. Alternatively, abnormal SWI/SNF complexes may disrupt the regulation of genes that help control the growth and division of cells, which leads to cancer. It is likely that other genetic changes in addition to *SMARCA4* gene mutations are necessary for cancer development.

Chromosomal Location

Cytogenetic Location: 19p13.2, which is the short (p) arm of chromosome 19 at position 13.2

Molecular Location: base pairs 10,960,922 to 11,062,282 on chromosome 19 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ATP-dependent helicase SMARCA4
- BAF190
- BAF190A
- brahma protein-like 1
- BRG1
- BRG1-associated factor 190A
- BRM/SWI2-related gene 1
- FLJ39786
- hSNF2b

- MRD16
- nuclear protein GRB1
- protein brahma homolog 1
- protein BRG-1
- RTPS2
- SMCA4_HUMAN
- SNF2
- SNF2-beta
- SNF2-like 4
- SNF2L4
- SNF2LB
- sucrose nonfermenting-like 4
- SWI2
- transcription activator BRG1

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): ATP-Driven Chromatin Remodeling Machines Change Nucleosome Structure
  https://www.ncbi.nlm.nih.gov/books/NBK26834/#A644
- Molecular Biology of the Cell (fourth edition, 2002): Chromosomal DNA and Its Packaging in the Chromatin Fiber
  https://www.ncbi.nlm.nih.gov/books/NBK26834/

GeneReviews

- Coffin-Siris Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK131811

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28SMARCA4%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- SWI/SNF-RELATED, MATRIX-ASSOCIATED, ACTIN-DEPENDENT REGULATOR OF CHROMATIN, SUBFAMILY A, MEMBER 4
  http://omim.org/entry/603254

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/SMARCA4ID42333ch19p13.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=SMARCA4%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=11100
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/6597
- UniProt
  http://www.uniprot.org/uniprot/P51532

Sources for This Summary

- Rodriguez-Nieto S, Cañada A, Pros E, Pinto AI, Torres-Lanzas J, Lopez-Rios F, Sanchez-Verde L, Pisano DG, Sanchez-Cespedes M. Massive parallel DNA pyrosequencing analysis of the tumor suppressor BRG1/SMARCA4 in lung primary tumors. Hum Mutat. 2011 Feb;32(2):E1999-2017. doi: 10.1002/humu.21415. Epub 2010 Dec 7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21280140
- OMIM: SWI/SNF-RELATED, MATRIX-ASSOCIATED, ACTIN-DEPENDENT REGULATOR OF CHROMATIN, SUBFAMILY A, MEMBER 4
  http://omim.org/entry/603254
- Tsurusaki Y, Okamoto N, Ohashi H, Kosho T, Imai Y, Hibi-Ko Y, Kaname T, Naritomi K, Kawame H, Wakui K, Fukushima Y, Homma T, Kato M, Hiraki Y, Yamagata T, Yano S, Mizuno S, Sakazume S, Ishii T, Nagai T, Shiina M, Ogata K, Ohta T, Niikawa N, Miyatake S, Okada I, Mizuguchi T, Doi H, Saitsu H, Miyake N, Matsumoto N. Mutations affecting components of the SWI/SNF complex cause Coffin-Siris syndrome. Nat Genet. 2012 Mar 18;44(4):376-8. doi: 10.1038/ng.2219.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22426308
- Wilson BG, Roberts CW. SWI/SNF nucleosome remodellers and cancer. Nat Rev Cancer. 2011 Jun 9;11(7):481-92. doi: 10.1038/nrc3068. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21654818

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